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LETTER TO THE EDITOR

Low-Dose Foscarnet Preemptive Therapy for Cytomegalovirus Viremia after Haploidentical Bone Marrow Transplantation

The use of haploidentical hematopoietic stem cell transplantation (haplo-HSCT) has increased steadily since its introduction by Powles et al. [1]. Although successful hematopoietic engraftment and control of acute graft-versus-host disease (aGVHD) through transplantation of mega-dose granulocyte colony-stimulating factor (G-CSF)–primed bone marrow grafts have been reported, immune reconstruction in recipients is usually delayed [2-5]. This might result from the use of an intensive conditioning regimen and a combination of several immunosuppressive agents in haplo-HSCT, resulting in a high rate of infections after transplantation. Among these infections, cytomegalovirus (CMV) is a major cause of morbidity and mortality. Prophylactic ganciclovir, either alone [6] or in combination with foscarnet [7], has been empirically used to prevent the development of systemic CMV infections. This approach is limited by the risk of treatment-associated neutropenia and/or renal toxicity, however. We report a preemptive therapy protocol designed to control CMV viremia after haplo-HSCT.

This study comprised 54 patients who underwent haplo-HSCT according to protocols described previously [2,4,5]. All of the patients and donors were negative for CMV-PP65 antigenemia detected with the CMV Brite reagent kit (Biotest Diagnostics, Denville, NJ). Once hematopoietic engraftment was achieved, peripheral blood samples were collected, and CMV pp65–positive cells were measured up to day 100 posttransplantation. For CMV infection prophylaxis, ganciclovir 10 mg/kg/day was administered starting on day 9 pretransplantation, followed by acyclovir 500 mg twice daily from day 1 to day 30 posttransplantation, then tapered to 600 mg/day orally for up to 6 months after transplantation. If CMV pp65–positive cells were detected, then foscarnet treatment was started at a dose of 60 mg/kg/day, with appropriate hydration maintained with 1000 mL saline solution/m^2 of body surface area. During foscarnet treatment, peripheral blood cell count, creatinine levels, and electrolyte concentrations were monitored.

CMV antigenemia occurred in 16 patients between day 30 and day 93 (median, 54 days) after transplantation. Among these 16 patients, 8 patients had fever, and 1 patient had fever with nausea, vomiting, and diarrhea and was diagnosed with CMV colitis. All 16 patients tested negative for CMV pp65 within 7 to 21 days (median, 12 days) after initiation of low-dose foscarnet therapy. In a 6- to 24-month follow-up, 1 patient tested positive for CMV pp65 again 12 months after transplantation. After treatment with gancyclovir, this patient was CMV pp65–negative. The patient with CMV colitis was treated with foscarnet 120 mg/kg/day for 2 weeks, after which the symptoms were controlled and the patient tested negative for CMV pp65.

During foscarnet treatment, 5 patients reported nausea and loss of appetite and 2 patients exhibited slight symptoms of urethral stimulation. No patient exhibited obvious changes in levels of electrolytes, creatinine, leukocytes, or platelets in peripheral blood. No patient developed irreversible renal or marrow failure.

Based on our findings, we recommend foscarnet as the first-line antiviral drug to prevent CMV infection in patients undergoing haplo-HSCT, which is associated with a higher rate of CMV viremia compared with HLA-identical HSCT. Low-dose foscarnet provides effective preemptive therapy for CMV antigenemia with acceptable toxicity.

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